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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/241,653	02/02/1999	HERMANN WAGNER	C1041/7002-H	8996

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EXAMINER	
ZARA, JANE J	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 09/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/241,653	WAGNER ET AL.	
	Examiner	Art Unit	
	Jane Zara	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-41,51-65,73 and 74* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-41, 51-65, 73,74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7-19-04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office action is in response to the communication filed 7-19-04.

Claims 27-41, 51-65, 73, 74 are pending in the instant application.

Response to Arguments and Amendments

The finality of the Office action mailed 5-5-04, and the allowability of claims 27-41, 51-64, 67, 68, 73 and 74 are hereby withdrawn upon further consideration and in light of the new rejections set forth below.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 27-32, 34-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 27, line 3, the descriptor "non-chemotherapeutic induced" is a parenthetical term, and it is unclear if this parenthetical term is meant to be a limitation of the claimed invention. If so, it should not be enclosed in parentheses.

In claim 31, line 1, "drug-induced" is used to describe thrombocytopenia. This limitation conflicts with the parenthetical limitation in claim 27 (i.e. "non-chemotherapeutic induced"). The metes and bounds of this claim cannot be determined, and claim 31 does not seem to further limit claim 27.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 27-41, 51-65, 73, 74 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for decreasing a reduction in platelet counts in a subject having drug induced or radiation induced thrombocytopenia, and a method for treating drug induced anemia comprising the administration of a CpG oligonucleotide comprising the sequence GACpGTT within 24 hours of the induction of thrombocytopenia or anemia, does not reasonably provide enablement for treating any form of thrombocytopenia or anemia, by increasing platelet counts or inducing erythropoiesis in a subject comprising the administration of any CpG containing oligonucleotide (and in any time frame relative to induction of thrombocytopenia or anemia). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are drawn to methods of increasing platelet counts in a subject having any induced form of thrombocytopenia, and methods of inducing erythropoiesis in a subject having any form of anemia comprising the administration of any CpG containing oligonucleotide of at least 8 nucleobases in length, at any time relative to the onset of thrombocytopenia or anemia.

The following factors have been considered in determining that the specification does not enable the skilled artisan to make and/or use the invention over the scope claimed.

The state of the prior art and the predictability or unpredictability of the art. CpG containing oligonucleotides are currently being investigated for exerting their immunotherapeutic effects in various organisms (See Krieg et al, Weiner and McCluskie et al for recent advances using CpG oligonucleotides). Biological responses to the administration of CpG containing oligonucleotides vary, however, depending on the mode and timing of administration and depending upon the organism (See McCluskie et al in its entirety, and especially on page 296; Also see Krieg et al on page 524). Weiner states furthermore that the molecular mechanisms of CpG oligonucleotides' immunostimulatory effects are not yet understood (See especially page 461). And while the biological effects of some chemical modifications have been studied for CpG containing oligonucleotides, such as 2'-O-methyl modifications, phosphorothioate internucleotide linkages and 5-methyl cytosine substitutions, the incorporation and positioning of chemical modifications relative to the CpG dinucleotide are highly

unpredictable (See Agrawal et al especially on pages 78-80; See also pages 31-32 of the instant specification).

The amount of direction or guidance presented in the specification AND the presence or absence of working examples. Applicants have not provided guidance in the specification toward a method of increasing platelet counts in a subject having any form thrombocytopenia or inducing erythropoiesis in a subject having any form of anemia comprising the administration of any CpG containing oligonucleotide at any time frame relative to onset of the thrombocytopenia or anemia, which conditions may be either chemically induced or non-chemically induced. Applicants have not shown guidance for increasing platelet cells because they have not provided any data indicating an increase in platelet precursor cells. The specification teaches an increase in splenomegaly, and increased GM-CFU (representative of granulocyte macrophage progenitor cells) in spleen cells and bone marrow cells in mouse models following the administration of CpG-1 or CpG-2 oligonucleotides. The specification also teaches a dose dependent increase in myeloid progenitor cells upon administration of increasing doses of CpG-1 or CpG-2 in a nude mouse model. The specification additionally teaches an reduced loss in splenic T cell, B cell, WBC and RBC counts in a mouse model of 5FU induced thrombocytopenia, wherein the CpG oligonucleotide was administered within approximately 24 hours of 5FU treatment.

One skilled in the art would not accept on its face the examples given in the specification as being correlative or representative of the successful treatment of any form of thrombocytopenia or anemia, including non chemically induced forms such as

autoimmune conditions, comprising the administration of any CpG containing oligonucleotide of at least 8 nucleobases, and administered at any time frame relative to induction of the thrombocytopenia or anemia, in view of the lack of guidance in the specification and known unpredictability associated with the ability to predict the biological effects exerted by any CpG containing oligonucleotides for treating these conditions and with no time frame constraints. The specification as filed fails to provide particular guidance which resolves the known unpredictability in the art associated with treating previously existing conditions of thrombocytopenia or anemia comprising the administration of any CpG oligonucleotide at any time or stage of the condition.

The breadth of the claims and the quantity of experimentation required. The claims are drawn to methods of increasing platelet counts in a subject having any induced form of thrombocytopenia, and methods of inducing erythropoiesis in a subject having any form of anemia comprising the administration of any CpG containing oligonucleotide of at least 8 nucleobases in length, at any time relative to the onset of thrombocytopenia or anemia. The results in the specification of a reduced loss of platelets or red blood cells following co-administration of 5FU and CpG-1 or 2 is not representative of the ability to treat any form of thrombocytopenia or erythropoiesis by administering any CpG at any time. Idiopathic thrombocytopenic purpura, for instance, is an auto-immune disorder that leads to the destruction of platelets because of anti-platelet antibodies existing in a subject. Radiation induced or 5FU induced thrombocytopenia or anemic conditions are not representative of all of the thrombocytopenia or anemic conditions claimed (e.g. the nude mouse models provided

in this study are not correlative or representative of the ability to treat an autoimmune disease by administering CpG oligonucleotides). The two examples of CpG provided in the instant disclosure (i.e. comprising the motif GACpGTT) are not representative of any CpG containing oligonucleotide. And the time frames of CpG administration relative to onset of the thrombocytopenia or anemia (e.g. co-administration of CpG with 5FU or administration of CpG-1 or 2 within 24 hours of onset of the condition) is not representative of the ability to treat this broad array of conditions by administering CpG oligonucleotides at any time during the disease or condition. It would require undue experimentation beyond that provided in the instant disclosure, or in the art, to enable the broad scope claimed.

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is **703-872-9306**. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(571) 272-0765.** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (571) 272-0760. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (571) 272-0564. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JOHN L. LeGUYADER
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

JZ
8-15-04